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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/998,716	11/30/2001	Alex J. Harvey	AV1 019	7210

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/998,716	HARVEY ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *38-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2002 and 21 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 30 November 2001. The preliminary amendments filed 19 February 2002 and 21 October 2003 have been entered. Claims 1-50 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-37) in the Paper filed 21 October 2003 is acknowledged. Claims 38-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 7 and 14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 2 of either one of copending Applications No. 10/463,980 or 10/351,196. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims merely expand the

scope of the conflicting claims in a nonspecific manner. The instant claim 7 generally encompass any DNA molecule comprising an isolated avian ovomucoid gene expression control region operably linked to a nucleic acid insert encoding a polypeptide and claim 14 limits the insert to encoding an interferon α2b polypeptide. One of the species set forth in claim 2 of the conflicting applications, which contain identical claim sets, is directed to a vector comprising a coding sequence and a promoter in operational and positional relationship to express said coding sequence in an avian oviduct, wherein said coding sequence is an interferon α 2b and wherein said promoter is an ovomucoid promoter. As this species is fully encompassed within the limitations of the instant claims, the genus claimed in the instant claims 7 and 14 would be obvious to one of ordinary skill in the art. Therefore the claims are unpatentable over claim 2 of either one of copending Applications No. 10/463,980 or 10/351,196.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Specification

The disclosure is objected to because of the following informalities: The brief description of Figure 3 refers only to SEQ ID NO: 1-25, while SEQ ID NO: 27 and 28 also appear in the figure.

The disclosure is also objected to because it contains an embedded hyperlink and/or other form of browser-executable code (e.g., page 16, line 10). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Objections

Claims 30-34, 36 and 37 are objceted to because of the following informalities: The claims, which are directed to a transformed cukaryotic cell, encompass non-clected subjcct matter. The specification at page 19, defines a transgenic animal as any animal in which one or more of the cells of the animal may contain a hetcrologous nucleic acid. Thus, to the extcnt that the eukaryotic cell of the claim might be comprised within an animal, thc claim reads on a transgenic animal. Furthermore, the claim is also directed to progeny of the cell, which clearly reads on a transgenic animal. The claim will therefore be examined only to the extent that it rcads on an isolated eukaryotic cell or a ccll in culture. The claim should be amended such that it no longer encompasses a cell *in vivo*. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 30 and 35-37 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. As the claims read on a transgenic animal (*Id.*) and thc claimed animal is not defined in such a way as to exclude a transgenic human, the claims read on a transgenic human, which is nonstatutory subject matter. Amending the claims to clearly indicate that the host cell and its progeny are "isolated" or "cultured" would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, the claims are directed to an isolated nucleic acid comprising an avian ovomucoid gene expression control region, various recombinant constructs and cells comprising said ovomucoid gene expression control region, and a method of using said ovomucoid gene expression control region to produce a protein. According to the discussion beginning at page 21, line 5 and continued through the first paragraph on page 24, the ovomucoid gene expression

eontrol region is a region located 5' to the transeription start site of a chicken ovomucoid gene and eomprising the nueleotide elements that are necessary for regulated expression of a downstream polypeptide-eneoding nueleic aeid. The elaims also eneompass variants of the ehieken promoter region set forth as SEQ ID NO: 26 including those ovomucoid gene expression eontrol regions found in turkey, duek, goose, quail, pheasant, ratite, ornamental bird or feral bird ovomucoid gene expression control region. Thus, the elaims appear to be generie to any ovomucoid gene expression control region found within a wide variety of avian speeies.

The Guidelines for Written Deseription state: "when there is substantial variation within the genus, one must deseribe a suffieient variety of speeies to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written deseription requirement for a elaimed genus may be satisfied through suffieient deseription of a representative number of speeies by aetual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying eharacteristics, i.e., structure or other physical and/or ehemieal properties, by funetional eharacteristies eoupled with a known or disclosed eorrelation between function and structure, or by a eombination of such identifying eharacteristies, suffieient to show the applicant was in possession of the elaimed genus" (MPEP §2163(3)(a)(ii)).

In the instant ease, the speeifieation provides a single example of an ovomueoid gene expression control region (i.e., the chieken ovomueoid gene expression control region set forth as SEQ ID NO: 26). There is no deseription of ovomucoid gene expression eontrol region as it oeeurs in any avian speeies other than ehieken or variants of the ovomueoid gene expression control region in ehicken other than that described by SEQ ID NO: 26. The general knowledge in the art eoneerning speeies variants of promoter sequences or alleles does not provide any speeifie

indication of how the structure of one allele obtained from one species is representative of other alleles within that species or promoter sequences within other species. The nature of alleles and species variants is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others such that possession of 1 can be viewed as possession of all. As the common attributes of the genus are not described, one of ordinary skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of nucleic acids encompassed by the ovomucoid gene expression control regions of the claims. Therefore, only the described nucleic acid comprising the sequence set forth as SEQ ID NO: 26 meets the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising the sequence set forth as SEQ ID NO: 26, does not reasonably provide enablement for any variant thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not

limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to an isolated nucleic acid comprising an avian ovomucoid gene expression control region, various recombinant constructs and cells comprising said ovomucoid gene expression control region, and a method of using said ovomucoid gene expression control region to produce a protein, wherein said ovomucoid gene expression control region is unlimited in structure or might be any variant of the sequence set forth as SEQ ID NO: 26.

State of the prior art and level of predictability in the art: The art generally teaches that the organization of *cis*-regulatory elements within promoters is highly complex and integrated. For example, according to the teachings of Arnone *et al.* (1997) *Development* 124:1851-1864 promoters are comprised of regulatory modules which are always found to contain multiple transcription factor target sites, and these contribute in various ways to the overall regulatory output (paragraph bridging pages 1851-1852). Arnone *et al.* further teaches that an underestimate of the number of diverse transcription factor interactions found within regulatory modules is approximately 6.2 (first full paragraph on page 1853). Still further, Arnone *et al.* teaches, "[t]here are no examples of regulatory modules serviced only by homeodomain proteins, or Zn finger proteins, and so forth. This suggests diversity in the nature of the protein:protein interactions that are required of the factors in order for each module to generate and

communicate its regulatory output" (second full paragraph on page 1853). Thus, given no more than the primary nucleic acid sequence of a region 5' to a coding sequence, the skilled artisan would have no idea how the sequence could be varied without destroying the function of the nucleic acid. The specification teaches, "the present invention is useful for the expression of an operably linked heterologous nucleic acid insert in a transfected avian cell" (page 4, lines 5-7). However, given the unpredictability of the art, the skilled artisan must rely on the specification to teach which of the nucleic acids encompassed by the claim could be used for that purpose without having to engage in undue experimentation.

Amount of direction provided by the inventor and existence of working examples: The specification provides the a single example of an ovomucoid gene expression control region (i.e., region upstream of the chicken ovomucoid coding sequence) and limits the promoter to comprising at least one avian CR1 repeat element and a proximal ovomucoid promoter (page 4, third paragraph). However, the requisite components that provide useful function of an ovomucoid promoter are undefined and no guidance is provided as to how the disclosed nucleic acid sequence might be varied such that the nucleic acid can still be used for the expression of an operably linked heterologous nucleic acid insert in a transfected avian cell short of blind trial and error experimentation.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to use the full scope of the claimed invention without first engaging in undue trial and error experimentation. The disclosure provides a single example of an ovomucoid gene expression control region which might be useful for expression of an operably linked

hcterologous nucleie acid insert. Applicant claims any variant of the sequence set forth as SEQ ID NO: 26 yet provides no information that would allow the skilled artisan to distinguish those nuclcic acid sequences that eould be used according to the teachings of the specification from those that could not be used without having to engage in blind trial and error experimentation to make and test each variant. Therefore, the skilled artisan would have to cngage in experimentation to use the full scope of the claimed invention.

Thus, due to thc art reeognized unpredietability of the struetural requirements for promotcr function and the lack of guidance in the specification or prior art with regard to how to distinguish the opcrative embodiments of the claimed invention, it would require unduc experimentation to make and use the invention eommensurate with the full scope of the claims.

The following is a quotation of thc second paragraph of 35 U.S.C. 112:

> Thc spccification shall conclude with onc or more claims particularly pointing out and distinctly claiming thc subject matter which thc applicant rcgards as his invention.

Claims 1-6, 10, 12, 21, 23 and 27-29 are rejected under 35 U.S.C. 112, seeond paragraph, as being indefinite for failing to particularly point out and distinctly claim thc subjeet matter which applicant regards as the invention.

Claims 1, 10 and 21 are indefinite in being directed to a "degenerate variant" of SEQ ID NO: 26. Thc phrase is not defined in the spccifieation and, as degeneracy is typically understood to refer to codon usage, it is unclear how it applies to a noncoding promoter sequenee. Claims 2-6 are indefinite insofar as they depcnd from claim 1 and claim 23 is indefinite insofar as it depends from claim 21.

Claims 12, 23, 28 and 29 are also indefinite beeause they recite limitations as derivatives of some starting material (e.g., a polyadenylation sequence derived from the SV40 virus or a cell

derived from an avian). Without a clear statement of the process by which the starting material is derivatized it is not possible to know the metes and bounds of such a limitation because any given starting material can have many divergent derivatives depending on the process of derivatization. This rejection could be overcome by amending the claim to substitute "isolated from" for "derived from".

Claim 23 is additionally indefinite in reciting "the polyadenylation signal". There is no antecedent basis for the polyadenylation signal in claim 21, from which claim 23 depends. Amending claim 23 to depend from claim 2 would be remedial.

Claim 27, and claims 28 and 29 as they depend therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The claim is directed to a method of expressing a heterologous polypeptide in a host cell, wherein the host cell is transfected with a recombinant DNA molecule limited only to comprising an ovomucoid gene expression control region. It would seem that the method would require that the recombinant DNA molecule must also comprise a nucleic acid encoding the heterologous polypeptide operably linked to the ovomucoid gene expression control region. Amending the claim accordingly would be remedial.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Please note: Art Unit 1636 will be moving to the new USPTO facilities on 14 January 2004. After that date, Examiner Sullivan can be reached at 571-272-0779 and Examiner Yucel can be reached at 571-272-0781.

DMS

DAVID GUZO
PRIMARY EXAMINER